IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	09/242,772
Applicant	:	WILLEM JAN MARIE VAN DE VEN et al.
Filed	:	June 25, 1999
Title	:	PLAG GENE FAMILY AND TUMORIGENESIS
Group Art Unit	:	1637
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Commissioner for Patents
P.O. Box 1450
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DECLARATION UNDER 37 C.F.R. § 1.132

I, Willem Jan Marie Van de Ven, declare as follows:

1. I am one of the named inventors of the invention described and claimed in the above-identified application.

2. I am a citizen of The Netherlands, and reside at Lei 8A/bus 42, B-3000 Leuven, Belgium. I graduated from the Katholieke Universiteit Nijmegen, currently known as Radboud Universiteit Nijmegen, and my employment history is as follows:

1973-1978	Research Fellow in RNA tumor virology, Department of Biochemistry (Head: Prof. Dr. H. Bloemendal), University of Nijmegen, The Netherlands.
1978-1979	Postdoctoral Visiting Fellow, Viral Genetics Section, (Head: Dr. J.R. Stephenson), Laboratory of Cellular and Molecular Biology (Head: Dr. S.A. Aaronson), National Cancer Institute, National Institute of Health, Frederick, Maryland, 21701, USA.

1979-1980	Scientist II, Viral Genetics Section (Head: Dr. J.R. Stephenson), Carcinogenesis Intramural Program, Frederick Cancer Research Center, Frederick, Maryland, 21701, USA. Fellow of the Royal Netherlands Cancer Foundation, KWF.
1980-1982	Head Research, Molecular Oncology Section, Department of Biochemistry (Head: Prof. Dr. H. Bloemendal), University of Nijmegen, The Netherlands. Scientist II, Laboratory of Viral Carcinogenesis and Control (Head: Dr. G.J. Todaro), Viral Genetics Section (Head: Dr. J.R. Stephenson), Carcinogenesis Intramural Program, National Cancer Institute, Frederick Cancer Research Center, Frederick, Maryland 21701, USA.
1982-1986	Head Research, Molecular Oncology Section, Department of Biochemistry (Head: Prof. Dr. H. Bloemendal), University of Nijmegen, Nijmegen, The Netherlands.
1986-1989	Associate Professor and Section Chief, Molecular Oncology Section, Department of Biochemistry (Head: Prof. Dr. H. Bloemendal), University of Nijmegen, Nijmegen, The Netherlands.
1988	Visiting Professor, Molecular Oncology Section, Center for Human Genetics, University of Leuven, Leuven, Belgium.
1989-present	Research consultant University of Nijmegen, The Netherlands.
1989-present	Professor, Laboratory for Molecular Oncology, Center for Human Genetics, University of Leuven & Flanders Interuniversity Institute for Biotechnology, Leuven, Belgium.
1990-1995	Program-director EC Concerted Action Program "Molecular Cytogenetics of Solid Tumors".
1992-1993	Program-director EC Bridge Program "Animal Cell Biotechnology".

3. I have read and am thoroughly familiar with the contents of the above-identified patent application as well as of the Nollet et al. reference cited in the Office Action dated November 19, 2004. I have read and I understand claims 53-58, which are defined as follows:

53. An isolated nucleic acid sequence consisting of 7313 base pairs as provided in SEQ ID N0 116 with an open reading frame of 1500 base pairs starting with the ATG at position 481-483 as provided in SEQ ID N0 116, wherein said open reading frame encodes for a pleomorphic adenoma gene 1 (PLAG1) protein.

54. An isolated hybrid nucleic acid sequence consisting of a fragment of the nucleic acid sequence according to claim 53 fused to a nucleic acid sequence comprised of a translocation partner of PLAG1, wherein the presence of said hybrid nucleic acid sequence allows the diagnosis of a cell containing said hybrid nucleic acid sequence as a tumor cell.

55. An isolated nucleic acid sequence according to claim 54, wherein said translocation partner is the CTNNB1 gene.

56. An isolated nucleic acid sequence according to claim 55 containing 509 base pairs corresponding to exon 1 of CTNNB1 fused to exons 3 to 5 of PLAG1.

57. An isolated nucleic acid sequence according to claim 55 containing 605 base pairs corresponding to exon 1 of CTNNB1 fused to exons 2 to 5 of PLAG1.

58. An isolated anti-sense nucleic acid sequence of the nucleic acid sequence according to claim 53 or fragments thereof which inhibit the expression of said nucleic acid sequence according to claim 53 in tumor cells.

4. As an expert in the field of molecular biology, I can attest that one skilled in the art would know how to design fragments of a specific gene sequence in general, and PLAG1 in particular, in order to diagnose the presence of a particular tumor cell without undue or burdensome experimentation, as protocols for nucleic acid fragment isolation of a gene sequence based on a specific function of the nucleic acid fragment are well known and commonly employed in the art.

5. I declare further that one skilled in the art would know how to design isolated hybrid nucleic acids consisting of a fragment of a specific gene sequence fused to a translocation partner or fragments thereof of the specific gene sequence in general, and PLAG1 and fragments thereof fused to CTNNB1 and fragments thereof, in particular, in order to diagnose the presence of a particular tumor cell without undue or burdensome experimentation, as protocols for fusing nucleic acids or fragments thereof to translocation gene partners or fragments thereof based on a specific function of the fused, i.e., hybridized, nucleic acid, are well known and commonly employed in the art.

6. I declare further that one skilled in the art would know how to design anti-sense nucleic acids and fragments thereof against nucleic acids, in order to diagnose the presence of a particular tumor cell without undue or burdensome experimentation, as protocols for anti-sense nucleic acids and fragments thereof of a specific gene sequence in general, and PLAG1 in particular, based on a specific function of the anti-sense nucleic acid or fragment thereof, e.g., inhibition of the expression of PLAG1, are well known and commonly employed in the art.

7. I declare further that the Nollet et al. reference is not prior art that anticipates the present invention because nowhere does Nollet et al. disclose an isolated nucleic acid sequence consisting of specific base pairs of PLAG1 located on exons 3 to 5 or fragments thereof fused to specific base pairs of a CTNNB1 gene located on exon 1 or fragments thereof, wherein the fused nucleic acid allows for the diagnosis of a cell as a tumor cell when it contains the hybrid nucleic acid sequence therein, and further wherein an isolated anti-sense nucleic acid sequence of the hybrid nucleic acid sequence or fragments thereof inhibit the expression of the hybrid nucleic acid sequence in tumor cells. Rather, the Nollet et al. reference solely discloses the determination of the primary structure of the CTNNB1 gene by analyzing cDNA and genomic clones, and makes no disclosure whatsoever of PLAG1 generally or to a hybridized nucleic acid consisting of PLAG1 fused to CTNNB1.

8. I declare further that all statements made herein of my own knowledge are true and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both,

under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any patent issuing thereon.

Willem Jan Marie Van De Ven

Date March 16th, 2005